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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,712	10/03/2003	Jillian Cornish	08987-009001 / 9900.99	9880

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EXAMINER	
BORGEEST, CHRISTINA M	
ART UNIT	PAPER NUMBER
1649	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/678,712	CORNISH ET AL.	
	Examiner	Art Unit	
	Christina Borgeest	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on *19 March 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12 and 19-27* is/are pending in the application.

4a) Of the above claim(s) *19,20 and 22* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,21,24,25 and 27* is/are rejected.

7)☒ Claim(s) *23 and 26* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

Formal Matters

The amendment filed 19 March 2007 is acknowledged. Claims 1-3, 5-9, 11, 12 and 21 are amended. Claims 13-18 is cancelled and claims 23-27 are new. Claims 19, 20 and 22 are withdrawn. Claims 1-12, 21 and 23-27 are under examination.

Rejections Withdrawn

Claim Rejections - 35 USC § 112, second paragraph

The rejection of claims 1-18 and 21 under 35 U.S.C. 112, second paragraph, as being indefinite is withdrawn in response to Applicants' amendment of the claims to recite what the effective amount of FGF-8, FGF-8 analog or FGF-8 agonist is effective to do.

Claim Rejections - 35 USC § 112, first paragraph

The rejection of claims 1-18 and 21 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a bone condition characterized by too little bone formation or for increasing or maintaining bone density or for stimulating osteoblast growth comprising administration of SEQ ID NO: 3, does not reasonably provide enablement for administration of FGF-8 variants, fragments or agonists for the treatment of any bone condition or modulating osteoblast

apoptosis or for the prevention of osteoporosis, osteopenia, bone defects or osteogenesis imperfecta as broadly claimed is withdrawn in part. Specifically, Applicants have addressed the Examiner's concern with the breadth of the term "bone condition" by adding the phrase "associated with excessive resorption or breakdown of bone tissue," thus this particular issue raised in the enablement rejection is resolved.

Furthermore, the rejection of claim 13 under 35 U.S.C. 112, first paragraph for reciting "modulating" osteoblast apoptosis in the alternative is withdrawn in response to Applicants' cancellation of that claim.

Finally, the rejection of claim 21 under 35 U.S.C. 112, first paragraph for reciting "preventing osteoporosis, osteopenia, bone defects or osteogenesis imperfecta" in the alternative is withdrawn in response to Applicants' amendment of that claim to delete "preventing".

The remaining issues under 35 U.S.C. 112, first paragraph are discussed below.

Claim Rejections - 35 USC § 102

The rejection of claims 1-18 and 21 under 35 U.S.C. 102(b) as being anticipated by Singh et al. (WO 01/00662, published 4 January 2001) is withdrawn in response to Applicants' amendment of the claims to recite "wherein FGF-8...is administered in an amount effective to treat the bone condition of the patient.

The rejection of claims 1, 3, 4, 5, 6, 7, 9, 10, 11, 12, 13, 15, 16, 17, 18 and 21 are rejected under 35 U.S.C. 102(e) as being anticipated by Khodadoust et al. (US PGPub:

20030022170, filed 29 March 2001) is withdrawn in response to Applicants' argument that SEQ ID NO: 11 (the sequence having over 90% identity with the sequences of the claimed methods) is not the sequence discussed in Khodadoust et al. as being effective at stimulating chondrocyte growth (see p. 13, 4th paragraph, and endnote in Applicants' Remarks). Furthermore, a text search of Khodadoust et al. reveals that SEQ ID NO: 11 is not mentioned or contemplated in the context of being used for stimulation of chondrocyte growth. The rejection is also withdrawn in response to Applicants' amendment of the claims to recite 90% (the sequences in Khodadoust that are contemplated for stimulation of chondrocyte growth have only about 60-75% similarity to the sequences recited in the claimed methods—see [0363] of Khodadoust et al.), thus the claims are now distinguished over the prior art.

Objections/Rejections Maintained

Claim Objections

The objection to claims 1-18 and 21 for reciting non-elected species (e.g., SEQ ID NOs: 1 and 2) is maintained for reasons of record and the following.

Applicants argue at p. 6, last paragraph that "upon allowance of a generic claim, Applicants will be entitled to consideration of claims to additional species which depend from or otherwise require all the limitations of an allowable generic claim." This argument has been fully considered but is not persuasive because no generic claims have been allowed.

Claims 23 and 26 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claim Rejections - 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The rejection of claims 1-18 and 21 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a bone condition characterized by too little bone formation or for increasing or maintaining bone density or for stimulating osteoblast growth comprising administration of an FGF-8 agonist polypeptide having at least 95% sequence identity to SEQ ID NO: 1, 2, or 3, does not reasonably provide enablement for administration of FGF-8 variants, fragments or agonists as broadly claimed is maintained for reasons of record and the following. In addition, new claims 24, 25 and 27 are hereby included in this rejection.

Applicants argue at p. 8, 3rd paragraph that Blunt et al. do not report the effects of FGF-8 or FGF-8 variants on osteoblasts or osteoclasts, thus their results fail to provide any evidence regarding enablement of the present claims.

Applicants argue at p. 9, 1st – 2nd paragraphs that the references cited by Examiner are not applicable to the present claims because the basis for using FGF-8 or

agonists thereof is not a mere function prediction, but rather Applicants have provided functional data showing biological effects on osteoblast proliferation and inhibition of osteoclast formation. Applicants' further argue that screening an agonist would be routine in view of the guidance provided in the specification and the teachings of the art.

These arguments have been fully considered but are not found persuasive. First, with regard to Applicants' comments about Blunt et al., the Examiner cited this reference to demonstrate that even FGF-8 analogs are not all capable of behaving in the same way; the reference need not teach the effect on osteoblasts and osteoclasts to be relevant, because the claims recite open language "comprising an amino acid sequence identical to the SEQ ID NO: 1, 2, or 3" and in the alternative, the claims recite any "fragment thereof comprising at least 10 amino acids of the sequence," thus encompass an enormous number of non-functional fragments. Case law directs that the presence of inoperative embodiments within the scope of a claim does not necessarily render a claim non-enabled. The standard is whether a skilled person could determine which embodiments that were conceived, but not yet made, would be inoperative or operative with expenditure of no more than is normally required in the art. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, 224 USPQ 409, 414 (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling). However, claims reading on significant numbers of inoperative embodiments would render claims non-enabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative. *Ibid.*; *In re Cook*, 439 F.2d 730, 735, 169 USPQ

298, 302 (CCPA 1971). Furthermore, the claims encompass ***treatment*** in a human patient, and not merely "screening an agonist" as the Applicants suggest at p. 9 of their arguments. Making and testing drugs capable of treating human patients is not routine and making and testing drugs is not the standard for enablement. Undue experimentation would be necessitated by the huge number of fragments and variants encompassed by the claims that would by necessity have to be tested for their efficacy in treatment of bone conditions characterized by excessive resorption or breakdown of bone tissue.

Furthermore, with respect to Applicants' arguments that the references cited by Examiner are not applicable to the present claims because the basis for using FGF-8 or agonists thereof is not a mere function prediction, and that Applicants have provided functional data showing biological effects on osteoblast proliferation and inhibition of osteoclast formation, Applicants have not provided functional data showing that every fragment or analog encompassed by the claims is capable of treating a bone condition associated with excessive resorption and breakdown of bone tissue. The claims are not commensurate in scope with the evidence provided by Applicants. Again, claims reading on significant numbers of inoperative embodiments would render claims non-enabled when the specification does not clearly identify the operative embodiments and undue experimentation is involved in determining those that are operative. *Ibid.*; *In re Cook*, 439 F.2d 730, 735, 169 USPQ 298, 302 (CCPA 1971). Because the claims encompass ***treatment*** in a human patient, and not merely "screening an agonist" as the Applicants suggest at p. 9 of their arguments, the standard for enablement is higher.

Making and testing drugs capable of treating human patients is not routine because undue experimentation would be necessitated by the huge number of fragments and variants encompassed by the claims that would by necessity have to be tested for their efficacy in treatment of bone conditions characterized by excessive resorption or breakdown of bone tissue.

Due to the large quantity of experimentation necessary to generate the infinite number of derivatives (variants, fragments, analogs or agonists) recited in the claims, and screen same for activity as a therapeutic agent for bone conditions, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function (not any 10mer fragment would be effective for treatment as recited in the claims), and the breadth of the claims which fail to recite any structural or functional limitations, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Conclusion

Claims 1-12, 21, 24, 25 and 27 are rejected. Claims 23 and 26 are objected to.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christina Borgeest whose telephone number is 571-272-4482. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Elizabeth C. Kemmerer

Christina Borgeest, Ph.D.

ELIZABETH C. KEMMERER, PH.D.
PRIMARY EXAMINER